

-continued

<223> OTHER INFORMATION: Xaa can be any naturally occurring amino acid

<400> SEQUENCE: 240

Cys	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Cys	Xaa	Xaa	Xaa	Xaa	Xaa	Cys	Xaa
1				5				10						15	
<hr/>															
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Cys	Xaa	Cys	Xaa
				20				25					30		
<hr/>															
Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Gly	Xaa	Arg	Cys					
				35			40								

1-16. (canceled)

17. A method of treating a cancer in a subject, wherein the cancer comprises cells having a mutation resulting in increased expression of a ligand for HER3, wherein the method comprises administering a therapeutically or prophylactically effective amount of an antigen-binding molecule which is capable of binding to HER3 to the subject, and wherein the antigen-binding molecule comprises:

- (i) a heavy chain variable (VH) region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:43

HC-CDR2 having the amino acid sequence of SEQ ID NO:46

HC-CDR3 having the amino acid sequence of SEQ ID NO:51; and

- (ii) a light chain variable (VL) region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:91

LC-CDR2 having the amino acid sequence of SEQ ID NO:94

LC-CDR3 having the amino acid sequence of SEQ ID NO:99.

18. The method according to claim 17, wherein the ligand for HER3 comprises an amino acid sequence having at least 60% sequence identity to the EGF-like domain of an NRG.

19. The method according to claim 17, wherein the mutation results in increased expression of the EGF-like domain of an NRG at the cell surface.

20. The method according to claim 17, wherein the cancer comprises cells having an NRG gene fusion.

21. The method according to claim 20, wherein the NRG gene fusion is selected from CLU-NRG1, CD74-NRG1, DOC4-NRG1, SLC3A2-NRG1, RBPMS-NRG1, WRN-NRG1, SDC4-NRG1, RAB21L1-NRG1, VAMP2-NRG1, KIF13B-NRG1, THAP7-NRG1, SMAD4-NRG1, MDK-NRG1, TNC-NRG1, DIP2B-NRG1, MRPL13-NRG1, PARP8-NRG1, ROCK1-NRG1, DPYSL2-NRG1, ATP1B1-NRG1, CDH6-NRG1, APP-NRG1, AKAP13-NRG1, THBS1-NRG1, FOXA1-NRG1, PDE7A-NRG1, RAB31L1-NRG1, CDK1-NRG1, BMPRII-NRG1, TNFRSF10B-NRG1, MCPH1-NRG1 and SLC12A2-NRG2.

22. The method according to claim 20, wherein the NRG gene fusion is selected from CLU-NRG1, CD74-NRG1, SLC3A2-NRG1 or VAMP2-NRG1.

23. The method according to claim 17, wherein the cancer comprises cells expressing HER3.

24. The method according to claim 17, wherein the cancer derives from the lung, breast, head, neck, kidney, ovary, pancreas, prostate, uterus, gallbladder, colon, rectum, bladder, soft tissue or nasopharynx.

25. The method according to claim 17, wherein the cancer is selected from lung cancer, non-small cell lung cancer, lung adenocarcinoma, invasive mucinous lung adenocarcinoma, lung squamous cell carcinoma, breast cancer, breast carcinoma, breast invasive carcinoma, head and neck cancer, head and neck squamous cell carcinoma, renal cancer, renal clear cell carcinoma, ovarian cancer, ovarian serous cystadenocarcinoma, pancreatic cancer, pancreatic adenocarcinoma, pancreatic ductal adenocarcinoma, prostate cancer, prostate adenocarcinoma, endometrial cancer, uterine carcinosarcoma, gallbladder cancer, cholangiocarcinoma, colorectal cancer, bladder cancer, urothelial bladder cancer, sarcoma, soft tissue sarcoma, neuroendocrine tumor and neuroendocrine tumor of the nasopharynx.

26. The method according to claim 17, wherein the cancer is selected from lung cancer, non-small cell lung cancer, lung adenocarcinoma, invasive mucinous lung adenocarcinoma and lung squamous cell carcinoma.

27. The method according to claim 17, wherein the antigen-binding molecule comprises:

- (i) a VH region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:41

HC-CDR2 having the amino acid sequence of SEQ ID NO:45

HC-CDR3 having the amino acid sequence of SEQ ID NO:48; and

- (ii) a VL region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:88

LC-CDR2 having the amino acid sequence of SEQ ID NO:92

LC-CDR3 having the amino acid sequence of SEQ ID NO:95.

28. The method according to claim 17, wherein the antigen-binding molecule comprises:

a VH region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:36; and

a VL region comprising an amino acid sequence having at least 70% sequence identity to the amino acid sequence of SEQ ID NO:83.

29. The method according to claim 17, wherein the antigen-binding molecule comprises:

a VH region incorporating the following framework regions (FRs):